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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/844,353	04/27/2001	Gary Ruvkun	00786/351005	3561

21559 7590 11/18/2003

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EXAMINER	
KAUSHAL, SUMESH	

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 11/18/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/844,353	RUVKUN ET AL.	
	Examin r	Art Unit	
	Sumesh Kaushal Ph.D.	1636	

-- Th MAILING DATE of this communication appears on th cov r sheet with the correspond nce address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 July 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2 and 4-15* is/are pending in the application.

4a) Of the above claim(s) *5-11* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4 and 12-15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Applicant's response filed on 07/28/03 has been acknowledged.

Claim 3 is canceled.

Claims 12-15 are newly filed.

Claim 1 is amended.

Claims 1-2, 4, 12-15 are examined in this office action.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The references cited herein are of record in a prior Office action.

► *Applicants are required to follow Amendment Practice under revised 37 CFR §1.121 (http://www.uspto.gov/web/offices/pac/dapp/opla/preognotice/revamdtprac.htm). The fax phone numbers for the organization where this application or proceeding is assigned is* ***703-872-9306.***

Election/Restrictions

This application contains claims 5-11 are drawn to an invention nonelected with traverse in Paper No. 7. A complete reply to the final rejection must include cancelation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Claim Rejections - 35 USC § 112

Claims 1-2, 4, 12-15 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed,

had possession of the claimed invention, for the same reasons of record as set forth in the office action mailed on 04/24/03.

Response to arguments

Applicant argues that the specification disclosed two human homologs of *C. elegans* daf-16 gene (FKHR and AFX) that are expected to function in human insulin signaling pathway. Applicant argues that the specification satisfied written description requirement in fig-13A and 13B where applicant disclosed two differentially spliced versions of daf-16 transcripts. In view of Dr. Ruvkun's declaration applicant further argues that daf-16 is so closely related to FKHR and AFX that they can replace daf-16 function in *C. elegans* (response, page 17-20). Accordingly the applicants concluded that they have satisfied written description requirement.

However, this is found NOT persuasive because scope of invention as claimed is not limited to a particular daf-16 gene defined by any structural and functional limitation. The scope of invention as claimed encompasses any natural and/or non-natural variant and/or homolog of daf-16 gene obtained from any organism. Applicant is referred to the guidelines for ***Written Description Requirement*** published January 5, 2001 in the Federal Register, Vol.66, No.4, pp.1099-1110 (see http://www.uspto.gov). Disclosure of a single species is rarely, if ever, sufficient to describe a broad genus, particularly when the specification fails to describe the features of that genus, even in passing. (see In re Shokal 113USPQ283(CCPA1957); Purdue Pharma L. P. vs Faulding Inc. 56 USPQ2nd 1481 (CAFC 2000). At best the applicant discloses that human AFX and FXHR are functional homologs of *C. elegans* daf-16 gene product. However, applicant fails to disclose any daf-16 gene obtained from any other organism that has at least 71% amino acid sequence similarity (29% variation) to SEQ ID NO:54 and has daf-16

like activity (i.e. regulation of insulin signaling pathway). The scope of invention as claimed encompasses a daf-16 like gene with at least 29% sequence variation, wherein the variation encompasses conserved motifs, which are required for daf-16 like activity. The earlier office action clearly provides the evidence that mere identification of critical regions would not be sufficient, as the ordinary artisan would immediately recognize that the encoded polypeptide must assume the proper three-dimensional configuration to be active, which is dependent upon the surrounding residues (see Ngo and Rudinger). Besides human AFX and FXHR the specification as filed fails to disclose any other daf-16 like gene sequences obtained form any other organism. One cannot describe what one has not conceived. See Fiddes v. Baird, 30 USP2d 1481 at 1483. In Fiddes, claims directed to a mammalian FGF's were found to be unpatentable due to lack of written description for that broad class wherein the specification provided only the bovine sequence. The possession may be shown by actual reduction to practice, clear depiction of the invention in a detailed drawing, or by describing the invention with *sufficient relevant identifying characteristics* (as it relates to the claimed invention as a whole) such that a person skilled in the art would recognize that the inventor had possession of the claimed invention. *See, e.g., Pfaff v. WellsElectronics, Inc., 525 U.S. 55, 68, 119 S.Ct. 304, 312, 48 USPQ2d 1641, 1647 (1998); Eli Lilly, 119 F.3d at 1568, 43 USPQ2d at 1406; Amgen, Inc. v. Chugai Pharmaceutical, 927 F.2d 1200, 1206, 18 USPQ2d 1016, 1021 (Fed. Cir. 1991).* In claims to genetic material, generic statement such as "vertebrate insulin cDNA" or mammalian insulin cDNA," without more, is not adequate written description of claimed genus, since it does not distinguish genus from others except by function, and does not specifically define any of genes that fall within its definition, or describe structural features commonly

possessed by members of genus that distinguish them from others; accordingly, naming type of material generally known to exist, in absence of knowledge as to what that material consists of, is not description of that material (*Eli Lilly, 119 F.3d at 1568, 43 USPQ2d at 1406)*. Similarly in the instant case daf-16 gene (as claimed) has been defined only by a statement of a function that broadly encompasses activation of insulin growth factor binding protein response element (see response page 19 and Dr. Ruvkun's declaration), which conveyed no distinguishing information about the identity of the claimed genetic sequence, such as its relevant structural or physical characteristics. According to these facts, one skill in the art would conclude that applicant was not in the possession of the claimed genus because a description of only one member of this genus is not representative of the variants of genus and is insufficient to support the claim.

Claims 1-2, 4 and 12-15 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for identifying a compound that decreases the expression or activity of *C. elegans daf-16* gene (AFX, FKHR) in a *C. elegans* or an isolated *C. elegans* cell, does not reasonably provide enablement for the method as claimed that requires the decrease in expression or activity of any variant and/or homologs of daf-16 gene obtained from all known organisms. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims for the same reasons of record as set forth in the office action mailed on 04/24/03.

Response to arguments

Applicant argues that the human homologs of the *C. elegans* daf-16 protein, FKHR and AFX are able to functionally substitute *C. elegans* daf-16 in vivo. Applicant argues that identification of other homologs of *C. elegans* daf-16 can be achieved using method described in the instant application, which is considered routine in the art (response page 21). Applicant argues that making a transgenic *C. elegans* is routine in the art and exhibit A provided an evidence that human homologs of neamtode daf-16 protein FKHR and AFX are able to functionally substitute for *C. elegans* daf-16 in vivo (response, page 23). Applicant argues that specification provides ample guidance to carry out the invention as claimed and it would not require any undue experimentation to exercise the invention as claimed, since such a screening is routine in the art (response page 24).

However, this is found NOT persuasive because the scope of invention as claimed is not limited to daf-16 gene that has been defined by any structural and functional limitation. The scope of invention as claimed encompasses any natural and/or non-natural variant and/or homolog of daf-16 gene obtained form any organism that could be used to screen candidate compounds for ameliorating or delaying an impaired glucose tolerance condition, atherosclerosis or obesity. Even though making a transgenic *C. elegans* is routine in the art making a transgenic *C. elegans* with any variant or homolog of daf-16, wherein the structure and function of the transgene has not been define is not considered routine in the art. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). In instant case screening of any and all natural and non-natural variants, wherein at least 29% amino acids are added substituted and/or deleted in the disclosed SEQ ID NO:54 is

not considered routine in the art, since making and testing a point mutation is significantly different from the making and testing an amino acid sequences wherein at least 29% amino acids are added, deleted and/or substituted. The number of possible scenario increase geometrically with increase in percent non-identity. Such making and testing is nothing more than an invitation to further experimentation, since the specification can not be relied on to teach how to make the variants as claimed. One has to engage in extensive making and testing in order to obtain variants that meet the functional requirements for the claimed daf-16 activity. This is not considered routine in the art and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). It is noted that the unpredictability of a particular area may alone provide reasonable doubt as to the accuracy of the broad statement made in support of enablement of claims. See Ex parte Singh, 17 USPQ2d 1714 (BPAI 1991). Therefore, one skill in the art would have to engage in excessive and undue amount of experimentation to exercise the invention as claimed.

Claim Rejections - 35 USC § 102

Claims 1-3, 4 stand rejected under 35 U.S.C. 102(b) as being anticipated by Gottlieb et al (Genetics 137:107-120, 1994) for the same reasons of record as set forth in the office action mailed on 04/23/03

Response to arguments

Applicant argues that the cited art does not teach a method to identify compounds that are capable of decreasing the expression of daf-16 gene (response page 25). Applicant argues that

the cited art only teaches a genetic pathway that control dauer formation (thin body worms) and fails to draw any connection between dauer pathway and obesity. Applicant argues that the cited art fails to identify any daf-16 nucleotide sequences and thus could not and did not produce a worm expressing daf-16 transgene (response, page 27). Applicant concluded that the cited art fails to teach important elements of the invention as claimed.

However, this is found NOT persuasive. The scope of invention as claimed does not require making of a worm expressing daf-16 transgene wherein the transgene has been identify by a nucleic acid sequence encoding a daf-16 gene. The invention as claimed is not limited to any particular nucleic acid sequences that encodes daf-16 gene. Limitations appearing in the specification but not recited in the claim are not read into the claim. In re Prater, 415 F.2d 1393, 1404-05, 162 USPQ 541, 550-551 (CCPA 1969). See also In re Zletz, 893 F.2d 319, 321-22, 13 USPQ2d 1320, 1322 (Fed. Cir. 1989). See also MPEP § 2111 - § 2111.01.

The cited art clearly anticipate a method for identifying a compound that modulates the expression and activity of *C. elegans daf-16 gene in C. elegans* (page 118, fig-4). Applicant fails to consider that the cited art teaches isolation of two new alleles of *daf-16* alleles (*m26, m27*) and construction of worms encoding *daf-16* wild-type or mutated *daf-16* transgenes (page 108, col1, para.2; pages 109-110). The cited art further teaches that to monitor the role of *daf-16* in dauer formation the worms were exposed to high pheromone/low food conditions in liquid media (page 113, col2, para.4). The cited art teaches the treatment of 10,0000 L1 worms with 5ul of pheremone (*a candidate compound*) at 25°C for 50-100 hours. The cited art teaches that *daf-16* is required both to initiate dauer formation as well as to maintain the dauer-differentiated state (page 114. col.1 para.1; page 115, fig-3). The cited art teaches that pheromone down regulates

both *daf-2 and daf-13* pathway, and other major daf-c pathways (page 114 col.1 para.3). The cited art further teaches that *daf-16* functions down stream of both *daf-2 and daf-23* (page 116, col.1 para.2). Based upon the data, the cited art presented a model to explain the function of *daf-2, daf-23* and *daf-16* in the regulation of dauer formation and continuous development (page 118, fig-4). The cited art teaches that up-regulation of *daf-2 and daf-23* down-regulate the *daf-16* expression. The high pheromone treatment down-regulates the daf-2 and daf-23 and up-regulates the *daf-16* expression (page 119, col.2, page 118, fig-4). Therefore the cited art clearly teaches a method that can identify a compound, which is capable of decreasing the expression or activity of *daf-16* gene (see page 118, fig-4). In addition, obesity is a relative term that is based upon body mass. Therefore the dauer-larvae, which have thin bodies are considered non-obese as compared to fat (obese) L3 worms (page 111, fig- 2, col.1 lines 12-15). Thus given the broadest reasonable interpretation the cited art clearly anticipate the invention as claimed.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sumesh Kaushal Ph.D. whose telephone number is 703-305-6838. The examiner can normally be reached on Mon-Fri. from 9AM-5PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Irem Yucel Ph.D. can be reached on 703-305-1998. The fax phone numbers for the organization where this application or proceeding is assigned is 703-872-9306. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

SKaushal
Patent examiner

JEFFREY FREDMAN
PRIMARY EXAMINER